

CLAIMS

What is claimed is:

1. A nucleic acid mimic in admixture with at least one target molecule selected from the group consisting of nucleic acids, transcription factors, carbohydrates and proteins, said mimic comprising a non-naturally occurring backbone structure to which are appended a plurality of heterocyclic bases, at least one of said bases being substituted with at least one sterically bulky substituent at a position one, two or three atoms removed from the position of attachment of said base to the backbone.
2. The nucleic acid mimic according to claim 1 wherein said sterically bulky substituent is $-R'$, $-OR'$, $-SR'$, $-N(R')_2$, $-C(R')_3$, $-C(=X)(R')$, $-C(=X)(-Y-R')$ or $S(=O)_{1-2}(-Y-R')$ wherein:
X is O, S or NH;
Y is O, S or NH; and
R' comprises at least 3 atoms and is H, C_1 - C_{50} -alkyl, C_2 - C_{50} -alkenyl, C_2 - C_{50} -alkynyl, C_7 - C_{50} -alkyl-aryl, C_6 - C_{50} -aryl, C_{10} - C_{50} -naphthyl, C_{12} - C_{50} -biphenyl, C_7 - C_{50} -aryl-alkyl, pyridyl, imidazolyl, pyrimidinyl, pyridazinyl, quinolyl, acridinyl, pyrrolyl, furanyl, thienyl, isoxazolyl, oxazolyl, thiazolyl and biotinyl, wherein R' can be substituted one or more times by $-NO$, $-NO_2$, $-SO_3^-$, $-CN$, $-OH$, $-NH_2$, $-SH$, $-PO_3^{2-}$, $-COOH$, $-F$, $-Cl$, $-Br$ and $-I$.
3. The nucleic acid mimic according to claim 1 wherein said base is a naturally or non-naturally occurring pyrimidine base.
4. The nucleic acid mimic according to claim 3 wherein said sterically bulky substituent is bound to C-6, C-5 or N-4 of said naturally occurring pyrimidine base.

5. The nucleic acid mimic according to claim 4 wherein said sterically bulky substituent is bound to N-4 of said naturally occurring pyrimidine base.

6. The nucleic acid mimic according to claim 5 wherein
5 said naturally occurring pyrimidine base is cytosine.

7. The nucleic acid mimic according to claim 5 wherein said sterically bulky substituent is (C=O)-R'' wherein R'' is C₁-C₂₀-alkyl or C₆-C₁₈-aryl.

8. The nucleic acid mimic according to claim 7 wherein
10 said sterically bulky substituent is (C=O)-C₆H₅.

9. A method for the determination of a nucleic acid comprising:

providing a nucleic acid mimic;

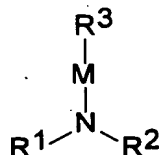
15 incubating said nucleic acid mimic and said nucleic acid under conditions suitable for the formation of a duplex between said nucleic acid mimic and said nucleic acid; and

determining the occurrence of said duplex as a measure of the occurrence of said nucleic acid;

20 said nucleic acid mimic comprising a non-naturally occurring backbone structure to which are appended a plurality of heterocyclic bases,

at least one of said bases being substituted with at least one sterically bulky substituent at a position one, two or three atoms removed from the position of attachment of said
25 base to the backbone.

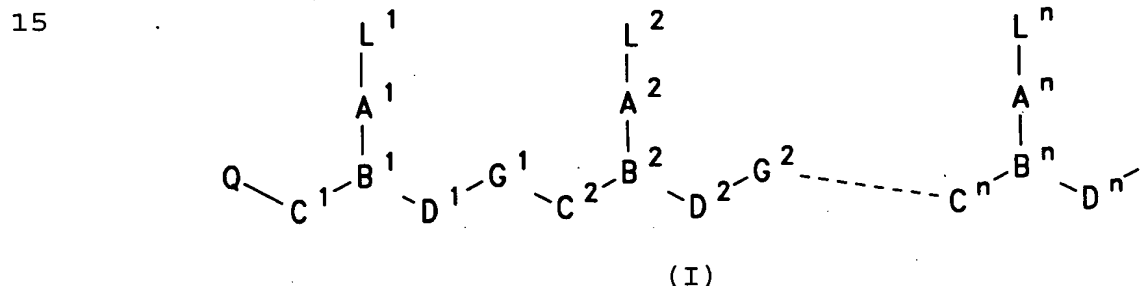
10. A compound for the preparation of a nucleic acid mimic having the general formula:



wherein:

- 5 R^1 is C_1 - C_4 -alkyl having at least one $-COOP^1$, $-NHP^1$, $-OP^1$ or $-SP^1$ group; P^1 is hydrogen or a protecting group;
 R^2 is C_1 - C_4 alkyl substituted by $-COOP^2$, $-NHP^2$, $-OP^2$ or $-SP^2$, wherein P^2 is hydrogen or a protecting group;
 M is a naturally or non-naturally occurring heterocyclic moiety
 10 bound to N by a one to three carbon linker; and
 R^3 is a sterically bulky substituent containing 3 or more non-hydrogen atoms.

11. The nucleic acid mimic according to claim 1 having formula (I):



wherein:

- n is at least 2,
 each of L^1 - L^n is independently selected from the
 20 group consisting of hydrogen, hydroxy, $(C_1$ - C_4)alkanoyl, naturally occurring nucleobases, non-naturally occurring nucleobases, aromatic moieties, DNA intercalators, nucleobase-binding groups, heterocyclic moieties, and reporter ligands, at least one of L^1 - L^n being said base substituted with at least
 25 one sterically bulky substituent;
 each of C^1 - C^n is (CR^6R^7) , where R^6 is hydrogen and R^7 is selected from the group consisting of the side chains of naturally occurring alpha amino acids, or R^6 and R^7 are

independently selected from the group consisting of hydrogen, (C₂-C₆)alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C₁-C₆)alkoxy, (C₁-C₆)alkylthio, NR³R⁴ and SR⁵, where R³ and R⁴ are as defined above, and R⁵ is hydrogen, (C₁-C₆)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C₁-C₆)alkyl, or R⁶ and R⁷ taken together complete an alicyclic or heterocyclic system;

each of D¹-Dⁿ is (CR⁶R⁷)_z where R⁶ and R⁷ are as defined above;

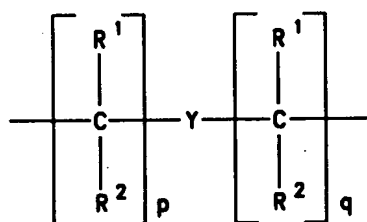
each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

each of G¹-Gⁿ⁻¹ is -NR³CO-, -NR³CS-, -NR³SO- or -NR³SO₂-, in either orientation, where R³ is as defined above;

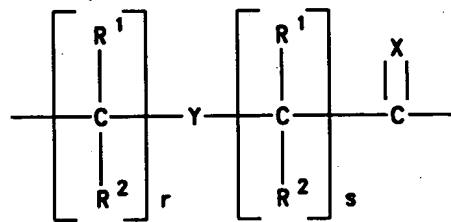
each pair of A¹-Aⁿ and B¹-Bⁿ are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R³N⁺; or

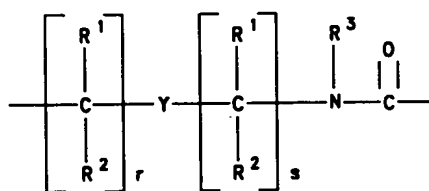
(b) A is a group of formula (IIId) and B is CH;



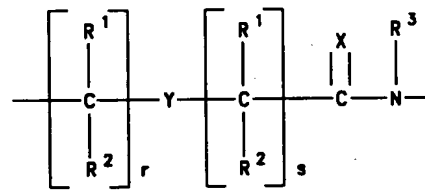
(IIa)



(IIb)



(IIc)



(IIId)

where:

X is O, S, Se, NR³, CH₂ or C(CH₃)₂;

Y is a single bond, O, S or NR⁴;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

each R¹ and R² is independently selected from the group consisting of hydrogen, (C₁-C₄)alkyl which may be

hydroxy- or alkoxy- or alkylthio-substituted, hydroxy, alkoxy, alkylthio, amino and halogen;

each of G^1-G^{n-1} is $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$ or $-NR^3SO_2-$, in either orientation, where R^3 is as defined above;

5 Q is $-CO_2H$, $-CONR'R''$, $-SO_3H$ or $-SO_2NR'R''$ or an activated derivative of $-CO_2H$ or $-SO_3H$; and

 I is $-NHR'''R''''$ or $-NR'''C(O)R''''$, where R' , R'' , R''' and R'''' are independently selected from the group consisting of hydrogen, alkyl, amino protecting groups,
10 reporter ligands, intercalators, chelators, peptides, proteins, carbohydrates, lipids, steroids, oligonucleotides and soluble and non-soluble polymers.

12. The nucleic acid mimic according to claim 11 wherein said target molecule is a nucleic acid.

15 13. The nucleic acid mimic according to claim 11 wherein said sterically bulky substituent is $-R'$, $-OR'$, $-SR'$, $-N(R')_2$, $-C(R')_3$, $-C(=X)(R')$, $-C(=X)(-Y-R')$ or $S(=O)_{1-2}(-Y-R')$ wherein:

 X is O, S or NH;

20 Y is O, S or NH; and

R' comprises at least 3 atoms and is H, C_1-C_{50} -alkyl, C_2-C_{50} -alkenyl, C_2-C_{50} -alkynyl, C_7-C_{50} -alkyl-aryl, C_6-C_{50} -aryl, $C_{10}-C_{50}$ -naphthyl, $C_{12}-C_{50}$ -biphenyl, C_7-C_{50} -aryl-alkyl, pyridyl, imidazolyl, pyrimidinyl, pyridazinyl, quinolyl, acridinyl,
25 pyrrolyl, furanyl, thienyl, isoxazolyl, oxazolyl, thiazolyl and biotinyl, wherein R' can be substituted one or more times by $-NO$, $-NO_2$, $-SO_3^-$, $-CN$, $-OH$, $-NH_2$, $-SH$, $-PO_3^{2-}$, $-COOH$, $-F$, $-Cl$, $-Br$ and $-I$.

 14. The nucleic acid mimic according to claim 11
30 wherein said base is a naturally or non-naturally occurring pyrimidine base.

15. The nucleic acid mimic according to claim 14 wherein said sterically bulky substituent is bound to C-6, C-5 or N-4 of said naturally occurring pyrimidine base.

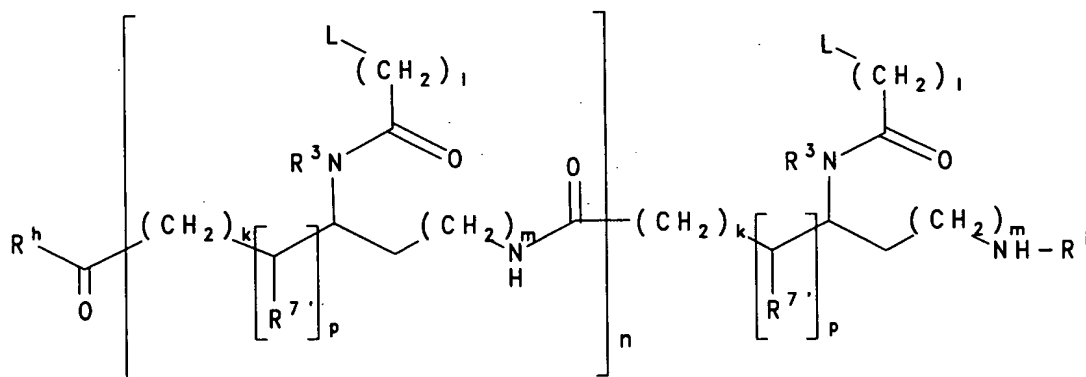
16. The nucleic acid mimic according to claim 15 wherein said sterically bulky substituent is bound to N-4 of said naturally occurring pyrimidine base.

17. The nucleic acid mimic according to claim 16 wherein said naturally occurring pyrimidine base is cytosine.

18. The nucleic acid mimic according to claim 16 wherein said sterically bulky substituent is (C=O)-R'' wherein R'' is C₁-C₂₀-alkyl or C₆-C₁₈-aryl.

19. The nucleic acid mimic according to claim 18 wherein said sterically bulky substituent is (C=O)-C₆H₅.

20. The nucleic acid mimic according to claim 11 having formula (IIIa):



(IIIa)

wherein:

each L is independently selected from the group consisting of hydrogen, phenyl, heterocyclic base moieties, including those substituted with a sterically bulky group or groups, naturally occurring nucleobases, and non-naturally occurring nucleobases, at least one L being said base substituted with at least one sterically bulky substituent;

each R'' is independently selected from the group consisting of hydrogen and the side chains of naturally occurring alpha amino acids;

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n is an integer from 1 to 60;
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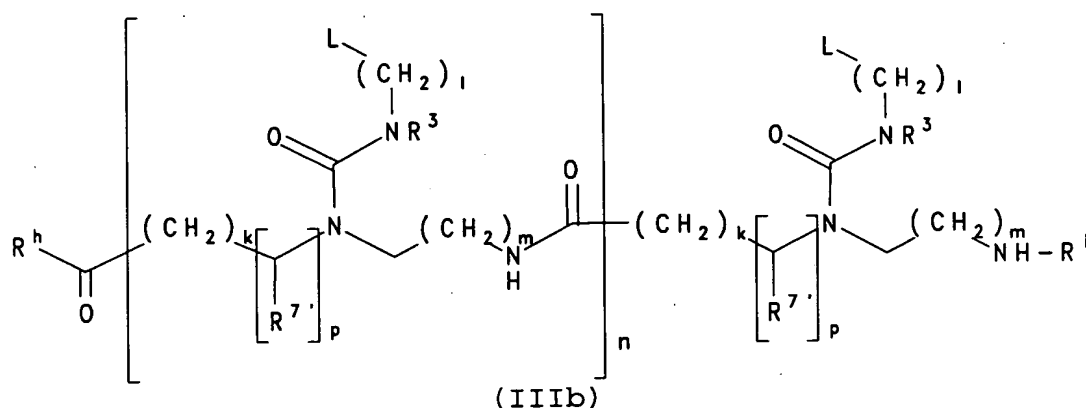
5 each of k , l , and m is independently zero or an
integer from 1 to 5;

p is zero or 1;

R^h is OH, NH₂ or -NHLysNH₂; and

$$R^i \text{ is H or } \text{COCH}_3.$$

10 21. The nucleic acid mimic according to claim 11
having formula (IIIb):



wherein:

each L is independently selected from the group consisting of hydrogen, phenyl, heterocyclic base moieties, including those substituted with a sterically bulky group or groups, naturally occurring nucleobases, and non-naturally occurring nucleobases, at least one L being said base substituted with at least one sterically bulky substituent;

each R^{7'} is independently selected from the group consisting of hydrogen and the side chains of naturally occurring alpha amino acids;

n is an integer from 1 to 60;

25 each of k, l, and m is independently zero or an
integer from 1 to 5;

p is zero or 1;

R^h is OH , NH_2 or $-NHLysNH_2$; and

R^i is H or COCH_3 .